ORIGINAL ARTICLE

Clinical significance of the neural response telemetric thresholds in Mandarin-speaking cochlear implant patients

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Abstract

Background: It is unclear whether neural response telemetric (NRT) thresholds are related to lexical tonal language performance after cochlear implants (CIs). We explored the factors associated with changes in NRT thresholds and postoperative performance of CI patients.

Methods: Patients receiving nucleus 24 CIs in our hospital from November 2010 were enrolled. We analyzed medical records and NRT thresholds. Mandarin speech and tone identification were measured in CI patients for at least 1 year postoperatively.

Results: Seventy-two patients with an average age of 16.1 years received CIs. The postoperative NRT threshold was lower than the intraoperative threshold. The NRT threshold was higher in the early- than the late-activation group (mapping within 21 vs >21 days postoperatively, respectively). Lower intraoperative NRT thresholds and curved electrodes were significantly associated with lower postoperative NRT thresholds. In multiple linear regression analysis, only postoperative NRT thresholds significantly affected speech and tone perception, including word recognition scores, tone perception, and comprehension of easy and difficult sentences (all $p < 0.05$). Other clinical parameters, including age, gender, implant type, and activation timing, were not significantly associated with clinical tone or speech outcomes.

Conclusion: Curved electrode arrays were associated with lower postoperative NRT thresholds. A lower postoperative NRT threshold might predict better performance of Mandarin-speaking CI patients. Future studies should evaluate factors that affect both postoperative NRT thresholds and lexical tonal language performance.

Keywords: Action potentials; Cochlear implants; Humans; Language; Speech

1. INTRODUCTION

Cochlear implants (CIs) are commonly used to treat severe-to-profound hearing loss in patients for whom conventional sound amplification is not helpful. However, speech perception in implanted patients shows variable improvements due to unclear reasons. Several related variables have been suggested to affect speech perception, including implant technology, socioeconomic status, anatomic abnormalities, and neuronal cell physiology and function.[1]

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Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2022) 85: 478-483.

Received September 22, 2021; accepted January 20, 2022.

doi: 10.1097/JCMA.0000000000000707.

The neural recording systems of CIs, which facilitate transcutaneous and bidirectional data transfer, play important roles in implantation and mapping.[2] Electrically evoked compound action potentials (ECAPs; also known as neural response telemetry [NRT] thresholds) facilitate intraoperative determination of device functionality and optimal electrode placement.[3] Animal studies have shown that ECAPs can be used to characterize the number and quality of spiral ganglion cells of the auditory nerve.[4,5] Compared with other electrophysiological measurements, such as electrically evoked auditory brain stem responses and electrically evoked cortical potentials, the advantage of ECAPs is that they are evoked by the cochlea itself and reflect the number and quality of the spiral ganglion cells, which constitute the interface between the implant and brain.[6] Recently, researchers and clinicians have explored whether it is feasible to use ECAP thresholds to objectively predict psychophysical outcomes and program speech processors.[7] Many studies have assessed the correlation between speech perception and ECAP recordings in CI patients.[8] However, few have focused on the association between competence in the use of a lexical tone language and data from ECAP recordings.

In this study, we analyzed changes in the NRT thresholds of various subgroups. We assessed the correlations of NRT measures and related variables with postoperative lexical tonal language performance, including tone recognition.

2. METHODS

2.1. Subjects

We enrolled 72 patients who received CIs in our hospital from November 2010. Patients with a history of psychological or cognitive impairment were excluded. All implants were unilateral. Hearing skills and Mandarin speech and tone perception were measured in 32 patients who had worn implants for at least 1 year and had a stable prognosis. This study was approved by the Institutional Review Board of the Chang Gung Medical Foundation (approval No. 105-0427C).

2.2. Cochlear implantation

All patients were operated on by the same surgeon (C.-F.H.). CIs were placed via standard cortical mastoidectomy, followed by posterior tympanotomy, using minimally invasive incisions. Curved electrodes (CI24RE and CI512) were inserted into the scala tympani after standard cochleostomy (1.5 mm). A round window approach or small cochleostomy (0.7 mm) was used to insert straight electrodes (CI422). All implants were manufactured by Cochlear Ltd (Sydney, Australia) and were from the Nucleus product range.

2.3. Electrophysiological recordings

ECAP measurements were recorded in the operating room immediately after CI and at the time of fitting. A speech processor was fitted after surgery, depending on the wound condition. The NRT software (AutoNRT; developed by Cochlear Ltd for use with the CI24) was used to measure ECAPs during the initial intra- and postoperative mapping. AutoNRT searches for thresholds by presenting a series of ascending and descending current levels (CLs). The maximum current stimulus was set to 255 CL. The threshold was defined as the mean of the lowest positive and highest negative response measurement.

2.4. Speech and tone perception

Four open-set speech and tone perception tests were used to examine all patients; the tests included an easy sentence test, difficult sentence test, phonetically balanced (PB) word recognition test, and Mandarin tone recognition test. The two sentence tests were based on the Central Institute for the Deaf Everyday Sentence test.[9] The easy sentence test included 15 sentences varying in length from 2 to 10 words. Each sentence contained one to seven key words chosen from a corpus of words familiar to all subjects, ie, words used in daily communication such as "book" and "car." The difficult sentence test consisted of 20 sentences varying in length from 2 to 12 words. Each sentence included 1 to 10 key words to be scored, but the words were less familiar to children (eg, "examine" and "dormitory"). The PB word recognition test included 25 monosyllabic words.[10] The Mandarin tone recognition test was developed and modified in a previous study.[11] The four Mandarin tones (flat, rising, dipping, and falling) were equally distributed throughout the word list. Four lists of monosyllabic words, each including 25 words that differed in tone, were used for tone identification. The scores corresponded to the percentage of correct identifications. Subjects were instructed to indicate their perceptions of the four tones either using hand motions or by pointing to graphical representations of the tones. Before the experiments, all subjects were trained to express their perceptions in these ways. The subjects were assigned scores based on the number of keywords correctly repeated; the numbers were converted to percentages before further analysis.[12] We used four lists of easy sentences and tones, three of difficult sentences, and five of PB words. The materials used for each test are shown in Supplementary Appendix 1 http://links.lww.com/JCMA/A140.

Auditory reception capacity and speech intelligibility were rated using the Categorical Auditory Performance (CAP) and Speech Intelligibility Rating (SIR) scales, respectively. The CAP was used to measure speech perception; this instrument assesses supraliminal performance, which reflects everyday auditory performance. A CAP score of 5 to 7 indicates some understanding of verbal language; scores of 0 to 4 indicate the extent of sound recognition but not language comprehension.[13] The SIR was used to measure speech intelligibility by quantifying the recognition of everyday spontaneous speech. The SIR is a time-effective, global outcome measure of speech intelligibility in real-life situations comprising five performance categories, ranging from 1 (pre-recognizable words in spoken language) to 5 (connected speech intelligible to all listeners).[14] All test procedures were the same as those of our previous report.[15]

2.5. Data analysis

Descriptive statistics were used to describe the clinical data and NRT thresholds and expressed as percentage, mean, and SDs. Parametric continuous data were analyzed using the Student's *t* test, paired samples *t* tests, and ANOVA test. Simple and multiple linear regression were used to evaluate the speech and tone tests in terms of the electrophysiological recordings, among other independent variables. Univariate and multivariate ordinary logistic regression models were used to evaluate ordinal data, including the CAP and SIR. All tests were two sided; the level of statistical significance was set at 0.05. All statistical analyses were performed with the MedCalc statistical software (version 17.5.5; MedCalc Software, Ostend, Belgium) and the SAS software (version 9.4; SAS Institute Inc, Cary, NC).

3. RESULTS

Of the 72 patients, 46 were male and 26 were female; the mean age at implantation was 16.16 years (range, 1–75 years). The demographic data are summarized in Table 1. The mean time from implantation to initial postoperative mapping was 16.7 days (range, 3–41 days).

3.1. NRT after early and "traditional" activation

In total, 13 ears were assigned to the E1 group (mapping within 7 days), 14 to the E2 group (7–13 days), 26 to the E3 group (14–21 days), and 19 to the traditional group (after 21 days). The NRT threshold decreased postoperatively, and a significant difference was evident between the initial intra- and postoperative recordings (Table 2). In contrast, no intraoperative group difference was observed in the NRT threshold. However, the NRT threshold in the early activation group (mapping within 21 days) was higher than that in the traditional group (mapping >21 days; 182.7 vs 169.3 CL, respectively; Student's *t* test; $p = 0.0156$).

3.2. Effects of electrode array and age

The intraoperative NRT threshold was not affected by the electrode array design or patient age (Table 2). Regarding the postoperative mapping recordings, the postoperative NRT threshold was significantly higher only in the group fitted with straight electrodes (Student's *t* test; $p = 0.0002$). Multiple linear regression of the postoperative data showed that the intraoperative NRT threshold and design of the electrode array significantly (both $p < 0.005$) affected the postoperative NRT threshold (Table 3).

3.3. Hearing and speech outcomes

For all 32 tested patients, all neural parameters, including the intra- and postoperative NRT thresholds, were evaluated in terms

Table 1

Clinical characteristics of 72 patients with cochlear implants

Characteristics	n (%)
Age, y (mean ± SD)	16.16 ± 20.57 (range, 1–75)
<18	n = 51 (70.8%); 5.03 ± 3.05 (range, 1–15.6)
≥18	n = 21 (29.2%); 43.17 ± 19.92 (range, 18–75)
Gender	
Male	46 (63.9%)
Female	26 (36.1%)
Implanted ear	
Left	39 (54.2%)
Right	33 (45.8%)
Implant type	
Curved (CI24RE/CI512)	28 (21/7) (38.9%)
Straight (CI422)	44 (61.1%)
Initial mapping days (mean ± SD)	16.69 ± 8.44 (range, 3–41)
NRT thresholds	
Intraoperative (mean ± SD)	197.0 ± 15.8 (range, 157.8–237.2 CL)
Postoperative (mean ± SD)	179.2 ± 20.9 (range, 128.7–236.8 CL)

CL = current level; NRT = neural response telemetry.

Table 2

Associations of various factors with NRT thresholds, as revealed by the intra- and postoperative mapping recordings

Variables	Intra-OP (mean ± SD)	*p*	Post-OP (mean ± SD)	*p*	*p* (intra/post-OP diff)
Initial mapping days		0.3349		0.0499[a]	
MAP < 7 (n = 13)	199.3 ± 14.9		182.1 ± 17.6		<0.0001[a]
7 ≤ MAP < 14 (n = 14)	202.9 ± 15.1		189.1 ± 17.8		0.0004[a]
14 ≤ MAP < 21 (n = 26)	194.9 ± 16.5		179.5 ± 24.5		<0.0001[a]
MAP ≥ 21 (n = 19)	194.0 ± 15.7		169.3 ± 16.5		<0.0001[a]
Age, y		0.6001		0.7397	
<18	197.6 ± 16.4		179.7 ± 22.8		<0.0001[a]
≥18	195.5 ± 14.3		177.9 ± 16.0		<0.0001[a]
Implant type	0	0.0638	0	0.0002[a]	
Curved (CI24RE/CI512)	192.7 ± 18.2		168.0 ± 20.7		<0.0001[a]
Straight (CI422)	199.8 ± 13.5		186.3 ± 17.9		<0.0001[a]

Diff = difference; MAP = mapping; NRT = neural response telemetry; OP = operative.
[a]$p < 0.05$.

Table 3

Relationships between various factors and the postoperative NRT thresholds, as revealed by multiple linear regression

Independent variables	Coefficient	SE	R^2 change	*p*
Intra-OP NRT	1.00	0.09	0.6661	<0.0001[a]
Age ≥18 vs <18 y	−1.93	3.66	0.0016	0.6010
Curved vs straight	−9.69	3.21	0.1847	0.0036[a]
Initial mapping days			0.1079	
MAP < 7 (reference)				
7 ≤ MAP < 14	1.50	4.76		0.7534
14 ≤ MAP < 21	1.18	4.67		0.8021
MAP ≥ 21	−3.36	4.96		0.5002

MAP = mapping; NRT = neural response telemetry; OP = operative.
[a]$p < 0.05$.

of their effects on the hearing and speech evaluation scores. The measurements were obtained at a mean of 43.2 ± 23.1 months after the operation (range, 12–90 months). In simple linear regression, both the intra- and postoperative NRT thresholds significantly affected speech and tone perception, including the word recognition scores, tone perception, and comprehension of easy and difficult sentences (all $p < 0.05$; Fig. 1). Other clinical parameters, including age, gender, implant type, and activation timing, were also evaluated; only implant type was significantly associated with word recognition, comprehension of difficult sentences, and the total score. After adjusting for interactions among the above variables in multiple linear regression, only the postoperative NRT threshold played a major role in the clinical outcomes of speech and tone recognition (Table 4).

The CAP and SIR are ordinal scales; therefore, the scores were subjected to ordinary logistic regression when measuring speech perception and intelligibility, respectively. In multivariate ordinary logistic regression, the CAP and SIR scores were significantly higher in the group with the lower postoperative NRT threshold (Table 5). In conclusion, a lower NRT threshold may indicate better speech performance.

4. DISCUSSION

We found that all the NRT thresholds, especially those of the initial postoperative mapping period, yielded valuable information on the relationships thereof with various clinical factors. Multiple linear regression revealed that a lower intraoperative NRT threshold and curved electrode arrays were associated with a lower NRT threshold in the postoperative mapping. However, only the postoperative NRT threshold significantly affected speech and tone recognition, indicating that a lower threshold may predict better performance in CI patients from regions with lexically tonal languages. This is the first study to identify associations between the neural data of CI patients and parameters of a lexically tonal language.

The NRT thresholds recorded intraoperatively were significantly higher than those recorded postoperatively at the time of initial stimulation (Table 2), in agreement with the findings of previous studies.[16,17] The differences may be attributable to physiological changes occurring within the cochlea between surgery and postoperative evaluation.[18,19] Postoperatively, the NRT thresholds were significantly higher in the group that received CI422 straight arrays (Table 3). This is explained by the proximity of the curved array to the modiolar wall, in agreement with previous findings,[18] and is consistent with the conclusion of Huang et al that the curved array (CI24RE) lies closer to the modiolus than the straight array.[20] However, this was not evident intraoperatively, perhaps because of the insertion technique used. A round window approach may lower the intraoperative NRT threshold,[21] intraoperatively offsetting the perimodiolar effect. Intraoperatively, the straight array was less invasive.

The speech perception of patients receiving CIs varied for unclear reasons; no simple method exists to predict the outcomes after implantation. ECAP data shed light on neuronal cell physiology and function, which may be important given the significant correlation between speech perception and the postmortem spiral ganglion cell count in the ears of CI patients.[6] A recent controlled study suggested that neural function is related to the postoperative performance after a CI.[22] However, a meta-analysis reported only weak evidence to support the use of ECAPs for CI fitting; ECAP thresholds are an equally weak predictor of both T and C levels.[23] In addition, a systematic review reported insufficient evidence that ECAP data predicted speech perception.[8] Considerable heterogeneity among studies and substantial shortcomings in study design were evident, which may have affected the study performance and the validity and generalizability of the results.

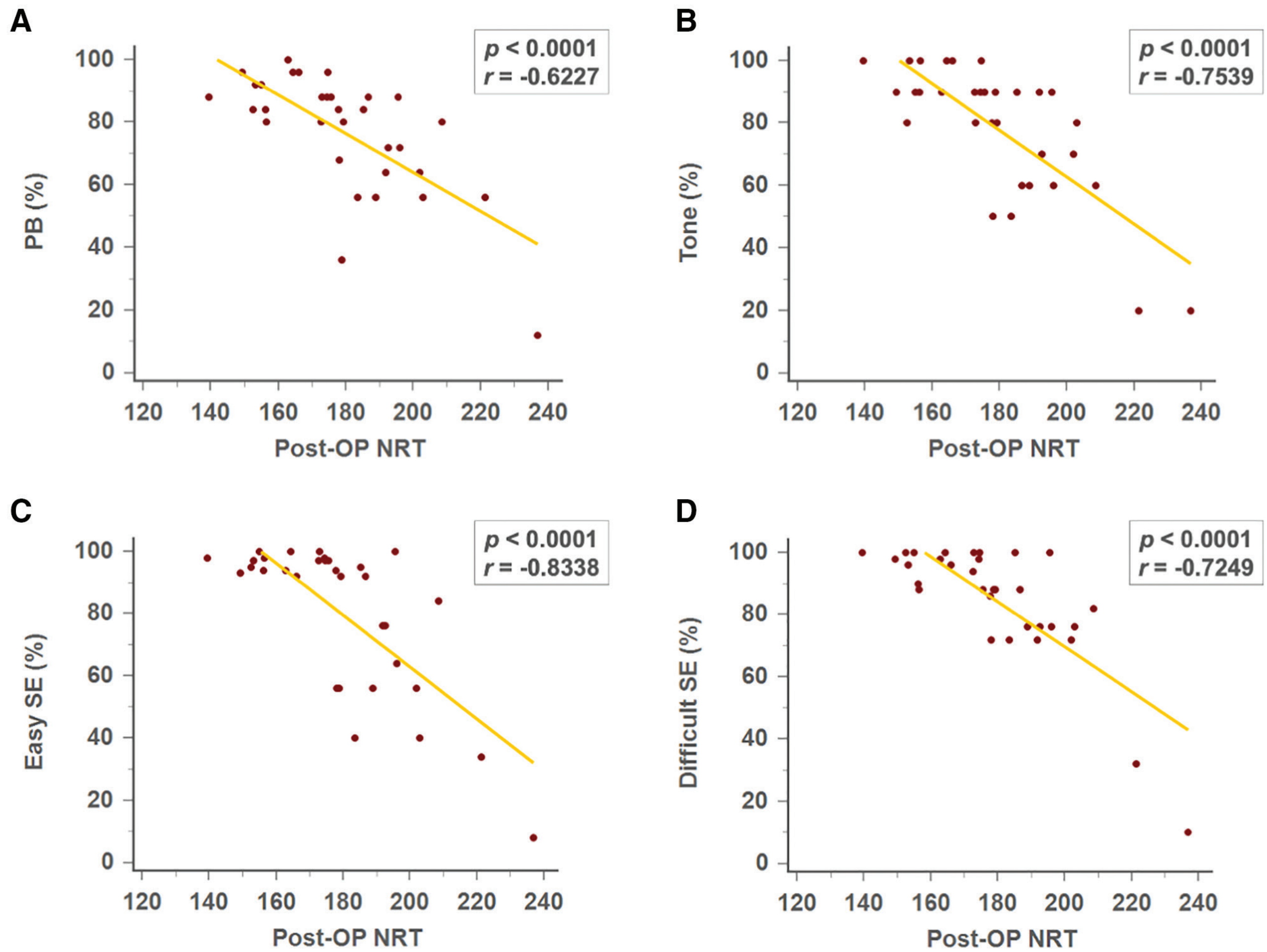

Fig. 1 Association between postoperative NRT threshold and speech performance. A, Phonetically balanced word. B, Tone. C, Easy sentence. D, Difficult sentence. NRT = neural response telemetry; OP = operative; PB = phonetically balanced word.

Appropriate outcome measures for patients speaking tonal languages (ie, ≥25% of the world's population) are urgently required. Mandarin—a lexical tonal language—conveys lexical meanings within syllables, in contrast to the changes in pitch used to express emotions in English. The CAP and SIR instruments have been used to explore the auditory performance and speech intelligibility of Mandarin-speaking prelingually deaf children receiving CIs.[24] Tonal information is particularly important in terms of tonal language and speech recognition; poor pitch discrimination poses a special challenge to Mandarin speakers with CIs. To date, little research has been devoted to this issue. Can speech perception and intelligibility in Mandarin, including tonal recognition, be predicted by electrophysiological measurements such as those of ECAP? We found that the postoperative NRT thresholds correlated significantly with the CAP, SIR, and speech perception scores, including for words, tones, and easy and difficult sentences. This indicated that a lower NRT threshold might predict better Mandarin speech performance. Intuitively, subjects with lower NRT thresholds are stimulated by lower volume sounds and should thus interpret speech better. This is the first study to explore the relationships between electrophysiological measurements and Mandarin speech performance. More studies on the relevant variables and outcome parameters are required for patients speaking tonal and nontonal languages.

Table 4

Multiple linear regression analysis of factors affecting speech/tone recognition (n = 32)

	PB (R^2 = 0.537)		Tone (R^2 = 0.621)		Easy SE (R^2 = 0.575)		Difficult SE (R^2 = 0.726)	
Variables	**b (SE)**	***p***	**b (SE)**	***p***	**b (SE)**	***p***	**b (SE)**	***p***
Age (≥18 = 1; <18 = 0)	−5.0 (6.1)	0.421	4.4 (6.1)	0.481	−5.1 (7.4)	0.493	6.5 (4.8)	0.186
Implant type (curved = 1; straight = 0)	−9.0 (6.1)	0.149	−0.9 (6.1)	0.878	−8.3 (7.4)	0.273	1.0 (4.8)	0.836
Intra-OP NRT	0.35 (0.26)	0.200	0.42 (0.27)	0.125	0.37 (0.32)	0.255	0.55 (0.21)	0.013[a]
Post-OP NRT	−0.86 (0.20)	<0.001[a]	−0.99 (0.20)	<0.001[a]	−1.08 (0.24)	0.001[a]	−1.01 (0.16)	<0.001[a]

NRT = neural response telemetry; OP = operative; PB = phonetically balanced word; SE = sentence.
[a]$p < 0.05$.

Table 5

Multiple ordinary logistic regression analysis of factors affecting the CAP and SIR scores (n = 32)

Variables	CAP multivariate OR (95% CI)	*p*	SIR multivariate OR (95% CI)	*p*
Age, y		0.282		0.791
<18	1		1	
≥18	2.720 (0.439–16.85)		0.795 (0.146–4.335)	
Implant type		0.065		0.795
Straight	1		1	
Curved	5.976 (0.897–39.84)		0.782 (0.123–4.982)	
Intra-OP NRT	1.066 (0.978–1.162)	0.147	1.032 (0.949–1.122)	0.463
Post-OP NRT	0.908 (0.843–0.979)	0.011[a]	0.908 (0.845–0.976)	0.009[a]

CAP = categories of auditory performance; NRT = neural response telemetry; OP = operative; OR = odds ratio; SIR = speech intelligibility rating.
[a] $p < 0.05$.

The influences of electrode type, length, and insertion depth on the speech comprehension were analyzed in previous studies.[25,26] Some previous studies have indicated that electrode length plays an important role in the ability to hear in difficult listening environments. CI manufacturers have developed thin and straight electrodes with lengths between 16 and 31 mm. The aim of these developments was to preserve residual hearing, even when it is marginal, by minimizing intraoperative damage to the sensitive intracochlear structures, while offering good speech understanding with electrical hearing only. In contrast, other studies have found no positive or negative correlation between insertion depth and speech understanding.[27] In brief, many different devices, electrode types, and surgical techniques have been investigated in previous studies, which have produced variable and complex results. In the present study, a curved electrode array is associated with a lower postoperative NRT threshold; we found that such a threshold predicted better comprehension of a lexical tonal language. However, this does not prove that a curved electrode is preferable to a straight electrode. Although a lower postoperative NRT threshold was significantly associated with better speech performance in multivariate analysis (Tables 4 and 5), the curved electrode array, which was associated with a lower postoperative NRT threshold, was not. The reason for this became apparent after multiple linear regression (Table 3). The intraoperative NRT threshold ($R^2 = 0.6661$) was the best-fitting parameter, followed by the type of electrode array ($R^2 = 0.1847$). In other words, the type of electrode array only partially explained the postoperative NRT threshold but did not explain the speech performance. In multivariate analysis, only the postoperative NRT threshold independently predicted better speech performance.

Our study had some limitations. First, a relatively small number of patients were evaluated in terms of speech and tone performance, making it difficult to draw robust conclusions. Second, we used two different devices (CI24RE and CI512) with the same curved array but different receiver designs; this may have affected the results. Finally, we used only nucleus devices; our data may thus not be applicable to other devices (Advanced Bionics; MED-EL).

In conclusion, curved electrode arrays were associated with lower postoperative NRT thresholds. A lower postoperative NRT threshold may predict better comprehension of a lexical tonal language. Future studies should evaluate factors that affect both postoperative NRT thresholds and lexical tonal language performance.

ACKNOWLEDGMENTS

This work was supported, in part, by grants from the National Science Council, Taiwan (MOST-109-2314-B-182A-015), Chang Gung Memorial Hospital Research Program (CMRPG8J1121 and CMRPG8J1301). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The authors thank the staff of the Speech and Audiology Department of the Chang Gung Memorial Hospital for their technical support.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://links.lww.com/JCMA/A140.

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